Advisory Committee on Blood Safety and Availability
January 28-29, 2004
SUMMARY OF MEETING

Inclement weather adversely affected member and speaker arrival and attendance. After a closed session, Celso Bianco, MD, Acting Chairman, called the meeting to order. The Executive Secretary reminded committee members and others wishing to speak to report actual or perceived conflicts of interest. A summary of previous Committee actions was not discussed in the absence of the chairman. The following were provided as updates to the Committee:

1. The Chair of the AABB-managed Interorganizational Task Force on Domestic Disasters and Acts of Terrorism described plans for a National Blood Reserve (NBR) to respond to sudden and unpredictable civilian or military needs blood, from loss of donors-donations or increased use.
    a. The NBR will consist of 10,000 units of liquid-stored red cells, blood types O, A and B normally distributed, and sequestered in designated military sites (2,000) or civilian exporting centers (8,000), prepared to ship within 4-6 hours.
    b. Ten thousand units will cover total supply loss in 2 major metropolitan areas and provide an immediate 3-day replacement.
    c. Every 2 weeks, the civilian reserve will be rotated to the export supply and replaced.
    d. Both the government and the private sector would share control of the reserve. Estimated start up cost is $2.59 M, followed by annual costs of $6.76M, mostly for blood acquisition.
    e. There must be a $10-$30M initial and follow-on national "awareness" campaign to encourage donors to give blood.

2. Dr Epstein (FDA) described the transmission in UK of variant Creutzfeldt-Jakob Disease (vCJD) by blood transfusion The FDA Transmissible Spongiform Encephalopathy Advisory Committee will review in February US preventative blood donor deferral strategies. Dr Ferguson (USDA) reported the first appearance bovine spongiform encephalopathy (BSE) in the US (Washington State), and measures to prevent further spread within this country.

3. Dr. Bowman (CMS) reported that the December 2003 Medicare Bill left blood and blood product reimbursement unchanged for now, but envisaged a transition to "average acquisition costs." Implementation rules were published in the Federal Register Jan 6 and 7, 2004. CMS will continue to seek hospital cost information (many transfusion costs are not billed or reported to CMS).

Main Meeting Topic: <u>The role of the government in the national blood supply (whole blood</u>

and plasma/plasma fractions) both in daily medical/surgical use and in local/national disaster.

1. The lead-off speaker, Dr. Sidney Wolfe, focused his health activist view of the US blood supply on the balance of interests and power between the Government, the Blood Industry and the public (patients). Whenever any two of these become too close, the resulting too little, too much or ill-focused regulation leads to performance problems. It is time, he said, for the blood industry to find solutions to the "predictable" blood shortage periods, e.g., summer, Christmas.

2. Dr Paul Schmidt reviewed the development and implementation of the National Blood Policy in the early 70s.
   a. Key elements included:
      i. eliminate paid donors;
      ii. collect data on blood banking and plasmapheresis;
      iii. encourage regionalization and resource-sharing;
      iv. make public the accounting for charges;
      v. support professional training and research, both basic and applied.

   b. The core values of the 1974 National Blood Policy was:
      i. supply,
      ii. quality,
      iii. accessibility, and
      iv. efficiency

3. In the absence of AABB President, Dr. Kathleen Sazama, Ms Karen Lipton, AABB Executive Director, reviewed a "National Blood Policy Forum" (May 3, 1999) to review the 1974 National Blood Policy. Priority issues were supply, data collection, education, research and adequate reimbursement. There should be cooperation/coordination in blood donation and blood centers should give consistent messages to donors. There was little consensus.

4. Dr. Jeffrey McCullough (UMN) surveyed blood banking in 18 developed countries in 1992-93 and updated much of it in early 2004. These countries collected 42.7-59.6 units/1,000 population (US, 53.6/M and Switzerland, an outlier, 88.4/M). Eleven professed to have a national program, but in only 5 did the responsible person-organization have authority over all technical and administrative activities. In general, the national organization coordinates, but production goals are fragmented, there is little inventory-sharing, there are multiple sources of funds and administration and management may be separate from operations. None met all criteria to match the characteristics of an ideal "national" program.

5. Canadian Blood Services (CBS) described by Dr. Graham Sher, CEO, was founded in 1998 following inquiries into the AIDS crisis of the 1980s and is fully funded by the Provinces (including a "contingency fund" to support advances in safety or other

technology). Provinces also support and control medical care, fostering cooperative comprehensive planning. They maintain a minimum 4 day supply of red cell products, and often have a greater cushion (7 days). Mutual trust fosters timely collection of blood center and hospital data that provides for an adequate supply, even to cope with loss of collections in one province. CBS uses paid advertising to support donor recruitment activities. Since 1998, the annual donations per donor has increased from 1.6 to more than 2.1, but only 3.6% of eligible donors donate each year, up from 3.0%.

6. Dr. Eilat Shinar described the blood services in Israel and the responses to disasters. Annually, they collect 45-50 red cell units per thousand people, which provides about a 2 day supply (they would prefer 3-5 days supply). The blood center supply is housed in 2 sites; most hospitals receive daily shipments and maintain a 3-5 day supply. Hospitals and the centers share inventory data before shipments are planned and made. Israel suffers 6,000 casualties per year in 1300 multi-casualty events, with 800 deaths. Two thirds of the casualties are mild, but more than 1250 are moderate to severe. From experience, they plan for 2-3 units per casualty and 7 units per moderate to severe casualty. Emergency Services relay information on multi-casualty events to the blood center and the receiving hospital, which confer about the need for anticipatory shipments. Last year, 15,000 units were requested and shipped in these circumstances and 9,000 were used. The public has responded well to maintain the supply and appeals are rarely needed. Blood Services sends plasma to a fractionator who supplies most of the albumin and immune globulins needed, but only 30% of the factor VIII used. The rest is imported, mostly from the US.

7. Mr Martin Gorham described the transformation of UK National Blood Services (NBS) beginning in 1995 into a national and nationalized operation to provide a "safe, sufficient and secure blood supply at an acceptable price." NBS is comprised of 4 integrated country blood services (England, Scotland, Wales and Northern Ireland). The NBS is an integral part of the National Health Service (NHS), which insures that centrally set fees from hospitals for products or services will support necessary costs. Inventory management is centralized and includes hospital input. National data collection allows fairly accurate planning and forecasting for needs. They try to have 50,000 units in stock (c. 6 days), consider 30,000 to be trouble and 70,000 too much and plan to manipulate collections within those ranges. The system has provided normal service despite the temporary loss of a blood center and planning is under way to cope with more massive disruptions. Resiliency has been added at the expense of some economies of scale. A government owned plasma fractionation plant supplies about 40% of the UK need. Since 1999, it has purchased US plasma for raw material. The remainder is from firms that meet standards.

Discussion:

1. Will sequestering blood in escrow compete with local hospital needs for blood?
   a. If the National Blood Reserve were supported by a 5-7 day supply of blood in

every locality, it would be very unlikely to compete with local demand.

b. A national blood donor awareness campaign is an essential underpinning to implementing a national reserve.

c. There was reluctance on the part of the Task Force to use the reserve as a weapon to resolve chronic or regional spot shortages, rather than keep it for true emergency situations.

d. The Task Force used the DHHS organ and tissue donation awareness campaign as its model for a similar campaign for blood donors.

e. For blood donations, the campaign probably needs to be on-going. PR campaigns are not of themselves very good at recruiting donors; the Task Force was said to have pointed out that the national campaign is separate from donor recruitment.

2. In case of catastrophe, would not sufficient blood be made available merely by canceling elective surgery?

   a. Ms Lipton stated that the largest use of blood today is for transplants (and cancer patients); postponing a transplant would likely cost an organ, already in short supply.

   b. A major problem in the US is lack of a system that could respond by shipping blood within 4 hours of a request. There likely is blood around, but mobilizing it for transport is a problem.

3. If every blood center/region had a 5-7 day supply of blood, would there be a need for a National Blood Reserve? There are insufficient data to answer this question.

4. The pros and cons of using frozen red cells for reserve was again debated, with pretty much the same solution; that is, on a national level, liquid stored reserves are more feasible and practical.

Second Day:

1. Mr. Brian O'Mahoney (World Federation of Hemophilia) modified the title of his presentation: "Hemophilia Treatment: A Global Perspective."

   a. Extrapolating from US figures (Hemophilia A 105 and B 28/M males); there are about 400,000 males with hemophilia, worldwide, of which just over 100,000 are diagnosed.

   b. He estimates that there are 600,000 individuals with von-Willebrand's Disease (vWD), of which less than 40,000 are recognized.

   c. Severely affected patients often die in childhood; milder cases can often survive with only trauma-induced bleeding. In developed countries (e.g., US, France, UK, Germany), therapy is generally available and more or less affordable.

   d. For emerging countries (e.g., Russia, Egypt, Iran, South Africa), most patients are diagnosed, but therapy is limited and quality of life poor. In less developed countries (e.g., India, China, Bangladesh, Indonesia), hemophilia is rarely diagnosed and viewed as rare and expensive to manage and may be largely

ignored.

e. Three quarters of the factor VIII used globally is used in developed countries; Less than 2% of the world's use of factor VIII is in the less developed countries.

f. Where there is a well conceived governmental plan to approach hemophilia, the proportion of patients with hemophilia diagnosed and given some treatment goes up, as well as survival, often dramatically. This can be started with much lower funding than is needed to provide near optimum treatment, which is expensive. He recommends a national tender and centralized purchasing to make therapy most efficient and cost-effective. Several countries were used as illustrative examples. Tender and central purchasing are not the only elements capable to reducing costs and increasing efficiency of care.

g. During the discussion period, the shrinking number of physicians qualified to treat patients with hemophilia in near optimal manner was pointed out. Physician staffing of Hemophilia Treatment Centers in the US is progressively more difficult. Other developed countries have less of a problem, but there is a shortage of expertise. The tender and centralized purchasing process was criticized as decreasing the incentives to bringing new or additional products to market, so that it might be counterproductive in the long run.

2. Dr. Louis Katz (Davenport, IA; President, America's Blood Centers) presented a view of the US Blood Banking "System," noting that it generally functioned well despite appearing somewhat disorganized. Most of the blood is collected by community blood centers (mostly Red Cross or ABC-members) that operate in similar fashion, supplying blood to their communities and by sharing from areas of plenty to pockets of need (7% or more). Some blood is collected by hospitals for their own purposes.

a. Hospitals are rarely self-sufficient, usually not FDA-licensed to ship blood interstate and less able to shift blood to where it might be needed.

b. The US blood supply is "incredibly safe" for which we should be proud, nevertheless, this comes at a cost, both financial and in loss of donors.

c. Blood use is increasing as the population increases and ages, but he estimated that 20-25% of the red cells transfused weren't really needed.

d. Geographic and other differences in practice (e.g., an Iowa hospital transfuses 93% of coronary by-pass patients; the VA system transfuses 43%) need to be explained.

e. Blood center inventories are decreasing, partly because they are shifting inventories to hospitals, which have the effect of cushioning them against the problems of shortages. It also reduces flexibility, since it is more complex to transfer blood between hospitals than it is to ship it from the blood center.

f. Donor recruitment must be increased and this requires funding. He noted a cooperative effort among the Ad Council, AABB, ABC and ARC to leverage nearly $2M to $30-$40M national prime time ad campaign to encourage donations from new and old donors and make them more receptive to calls from the local blood center.

g. He described the ABC "Stoplight" program as the first national public real-time

supply monitor, one of whose goals is to promote resource sharing between ABC members.

h. Disconnect between safety issues were discussed, largely managed and ultimately mandated by FDA and CMS, which controls reimbursement. Adding funds to blood-using Disease Related Groups DRGs do not necessarily translate to a hospital willing to pay more for the safety and other improvements in transfusion practice. The highest priority for government involvement is promoting blood donation as a civic responsibility. If you ask eligible individuals, they will donate. Asking them in a fashion that they know they have been asked is costly. This translates into more money ("new money"), primarily for donor recruitment.

3. Dr Jonathan Goldsmith (Immune Deficiency Foundation) addressed 3 topics:
   a. access to care as influenced by supply and reimbursement policies;
   b. classification of immune globulin products, generic or not; and
   c. a need for new research initiatives to improve future care for immune deficient patients.

   Recent reductions in reimbursement rates for out-patient infusion of IV immune globulin (IVIg) have caused some hospitals to reduce or discontinue their provision of this service, with an adverse affect on patient care. CMS classifies IVIg as a "drug" rather than as a blood product. This reduces the potential for selection based upon patient and IVIg product differences because it allows only "generic" IVIg.

   In September 2003, a US Immunodeficiency Network (USIDNET) was established by a consortium of investigators and supported by NIH. USIDNET objectives are study clinical, molecular and cellular characteristics of genetically determined immunodeficiency diseases, to identify the molecular basis for newly defined primary immune deficiency diseases, to improve the diagnostic tools for these diseases, to advance novel therapeutic approaches to their therapy and to encourage the use of disease registries and repositories of DNA and cells. There are relatively few laboratories now able to diagnose immune deficiency diseases and only those accredited under CLIA can begin to levy fees for that diagnostic service.

4. Christopher Healey (Plasma Protein Therapeutics Association – PPTA) discussed the importance of access and choice by patients for appropriate plasma product therapy. Although raw material safety is important, the focus should be more on end product safety. For example, fractionation and viral inactivation procedures have been shown by model virus testing to prevent infectious West Nile Virus from contaminating end products. This should obviate the need for extensive and expensive studies of the WNV itself. The need for and the design of clinical trials to support uncommon indications for the use of IVIg should be reevaluated. He supported Dr. Goldsmith's concern about reimbursement policies and their effect on access to care. Many plasma therapies are unique to the manufacturer and applying the generic label does not take into

consideration differences in the donor base and particular manufacturing processes.

5. Ms Teresa Lee (Associate Vice President for Payment and Policy, Advanced Medical Technology Association – AdvaMed) spoke on behalf of medical technology innovators and manufacturers worldwide. She encouraged the Committee to include adequate CMS reimbursement for blood in any recommendations for blood policy. AdvaMed supports the efforts by AABB and others to improve hospital billing and reporting practices with regard to blood. They also support the efforts toward disaster preparedness with equipment and supplies to collect, process and ship blood and blood products.

6. Ms Theresa Wiegmann (Director of Public Policy and Counsel to the AABB) described the introduction of West Nile Virus (WNV) testing in record time as a model of public-private cooperation. This safety measure probably prevented more than 1,000 transfusion transmitted WNV infections. Much attention to infectious complications of blood transfusion has made transfusion transmitted virus disease a rare event. It is now time to devote attention and energy to non-infectious complications of transfusion, namely errors resulting in the transfusion of the wrong unit to the wrong patient. Dr. Sandler supports the need to address this issue, noting that his hospital (Georgetown) successfully piloted a bar-code based system. To implement this system hospital-wide would take $1M. Dr. Heaton noted that his company (Chiron) was studying technology to convert all red cells to blood group O. Ms Wiegmann also added her voice to the call for Federal support of a public education campaign to encourage people to donate blood.

General Discussion: Dr. Holmberg stated that the purpose of the discussion was to set out a road map for Committee deliberations and actions for the next couple of years. Recent recurrent issues for the Committee have been monitoring the blood supply, donor recruitment, reimbursement, look back for possible hepatitis C infections, and unsolved problems in transfusion safety (e.g. new viruses such as West Nile; transfusion errors)

After wide-ranging discussion, the following was moved (Dr Heaton) and seconded (Dr. Sandler):

Whereas, the DHHS ACBSA finds that current instability in the national blood system poses threats to blood safety and availability and limit national preparedness to address disasters, including potential acts of terrorism; and whereas, the Committee finds that the goals of supply, quality, accessibility and efficiency, as stated in the 1974 national blood policy remain applicable; the Committee recommends that DHHS urgently:

1) take steps to enable development of a 5-7 day inventory of blood components in all collection centers, both to stabilize the blood system and to improve preparedness for disasters;
2) fully fund the DHHS Blood Action Plan, especially in the area of private and government supply monitoring, and increasing the blood supply;
3) address funding needs at all levels of the blood system to support product safety, quality, availability and access through targeting of additive resources and appropriate

reform of the CMS reimbursement system for blood and blood products, including plasma-derived therapeutics or therapies and their recombinant analogues.

And whereas, consistent with our previous recommendations of January 2002, the ACBSA further believes that establishing a national blood reserve program would add stability and security to the US blood system, if developed in the context of expanded daily collection inventories through an enhanced program to expand and sustain volunteer blood donations; and whereas the Committee additionally endorses the elements of the national blood reserve program, as developed by the AABB Interorganizational Task Force, therefore, the Committee also recommends that

4) DHHS fund development of a national blood reserve as a government-private sector partnership.

Submitted by:

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Certified by:

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